

WHAT IS CLAIMED IS:

1. A formulation comprising:
  - (a) a therapeutically effective amount of levomepromazine or a pharmaceutically acceptable salt thereof,
  - (b) ethylenediaminetetraacetic acid (EDTA) or a pharmaceutically acceptable salt thereof as a first stabilizer, and
  - (c) monothioglycerol (MTG) or glutathione as a second stabilizer, wherein said stabilizers are present in an amount effective to stabilize said formulation, and wherein said formulation is subjected to sparging.
2. The formulation of claim 1, wherein said second stabilizer is MTG.
3. The formulation of claim 1, wherein said second stabilizer is glutathione.
4. The formulation of claim 1, wherein said formulation is substantially free of sulfite compounds.
5. The formulation of claim 1, wherein said formulation is terminally sterilized.
6. The formulation of claim 5, wherein said formulation is terminally sterilized by autoclaving.
7. The formulation of claim 1, wherein each of said stabilizers is present in an amount of from about 0.001% to about 5% by weight per volume of the formulation.

8. The formulation of claim 7, wherein said amount of EDTA or a pharmaceutically acceptable salt thereof is about 0.02% to about 0.2% by weight per volume of the formulation.
9. The formulation of claim 7, wherein said amount of MTG or glutathione is about 0.05% to about 2% by weight per volume of the formulation.
10. The formulation of claim 1, wherein said formulation contains a concentration of total impurities of less than about 3% by weight per volume of the formulation.
11. The formulation of claim 1, wherein said formulation contains a concentration of the impurity levomepromazine sulfoxide of less than about 2% by weight per volume of the formulation.
12. The formulation of claim 5, wherein said formulation contains a concentration of total impurities of less than about 3% by weight per volume of the formulation.
13. The formulation of claim 5, wherein said formulation contains a concentration of the impurity levomepromazine sulfoxide of less than about 2% by weight per volume of the formulation.

14. The formulation of claim 1, further comprising a pH buffering agent in an amount sufficient to buffer the formulation to a pH in the range of from about 3 to about 7.

15. The formulation of claim 14, wherein said pH is in the range of from about 4 to about 5.5.

16. The formulation of claim 14, wherein said pH buffering agent comprises citric acid or a pharmaceutically acceptable salt thereof.

17. The formulation of claim 1, wherein said formulation is substantially oxygen-free.

18. The formulation of claim 1, wherein said formulation is suitable for parenteral administration.

19. The formulation of claim 18, wherein said parenteral administration comprises injection.

20. The formulation of claim 18, wherein said formulation is contained in a container selected from the group consisting of a vial, a syringe and an ampoule.

21. A formulation comprising:

(a) a therapeutically effective amount of levomepromazine or a pharmaceutically acceptable salt thereof,

- (b) ethylenediaminetetraacetic acid (EDTA) or a pharmaceutically acceptable salt thereof as a first stabilizer,
  - (c) monothioglycerol (MTG) or glutathione as a second stabilizer, and
  - (d) ascorbic acid or a pharmaceutically acceptable salt thereof as a third stabilizer,
- wherein said stabilizers are present in an amount effective to stabilize said formulation.

22. The formulation of claim 21, wherein said formulation is subjected to sparging.

23. The formulation of claim 21, wherein said second stabilizer is MTG.

24. The formulation of claim 21, wherein said second stabilizer is glutathione.

25. The formulation of claim 21, wherein said formulation is substantially free of sulfite compounds.

26. The formulation of claim 21, wherein said formulation is terminally sterilized.

27. The formulation of claim 26, wherein said formulation is terminally sterilized by autoclaving.

28. The formulation of claim 21, wherein each of said stabilizers is present in an amount of from about 0.001% to about 5% by weight per volume of the formulation.

29. The formulation of claim 28, wherein said amount of EDTA or pharmaceutically acceptable salt thereof is about 0.02% to about 0.2% by weight per volume of the formulation.

30. The formulation of claim 28, wherein said amount of MTG, glutathione, or ascorbic acid or a pharmaceutically acceptable salt thereof is about 0.05% to about 2% by weight per volume of the formulation.

31. The formulation of claim 21, wherein said formulation contains a concentration of total impurities of less than about 3% by weight per volume of the formulation.

32. The formulation of claim 21, wherein said formulation contains a concentration of the impurity levomepromazine sulfoxide of less than about 2% by weight per volume of the formulation.

33. The formulation of claim 26, wherein said formulation contains a total concentration of impurities of less than about 3% by weight per volume of the formulation.

34. The formulation of claim 26, wherein said formulation contains a total concentration of the impurity levomepromazine sulfoxide of less than about 2% by weight per volume of the formulation.

35. The formulation of claim 21, further comprising a pH buffering agent in an amount sufficient to buffer the formulation to a pH in the range of from about 3 to about 7.

36. The formulation of claim 35, wherein said pH is in the range of from about 4 to about 5.5.

37. The formulation of claim 35, wherein said pH buffering agent comprises citric acid or a pharmaceutically acceptable salt thereof.

38. The formulation of claim 21, wherein said formulation is substantially oxygen-free.

39. The formulation of claim 21, wherein said formulation is suitable for parenteral administration.

40. The formulation of claim 39, wherein said parenteral administration comprises injection.

41. The formulation of claim 39, wherein said formulation is contained in a container selected from the group consisting of a syringe, a vial and an ampoule.

42. A formulation comprising:

- (a) a therapeutically effective amount of levomepromazine or a pharmaceutically acceptable salt thereof,
- (b) ethylenediaminetetraacetic acid (EDTA) or a pharmaceutically acceptable salt thereof as a first stabilizer,
- (c) ethylgallate or cysteine as a second stabilizer, and
- (d) ascorbic acid or a pharmaceutically acceptable salt thereof as a third stabilizer,

wherein said stabilizers are present in an amount effective to stabilize said formulation, and wherein said formulation is subjected to sparging.

43. The formulation of claim 42, wherein said second stabilizer is ethylgallate.

44. The formulation of claim 42, wherein said second stabilizer is cysteine.

45. The formulation of claim 42, wherein said formulation is substantially free of sulfite compounds.

46. The formulation of claim 42, wherein said formulation is terminally sterilized.

47. The formulation of claim 46, wherein said formulation is terminally sterilized by autoclaving.

48. The formulation of claim 42, wherein each of said stabilizers is present in an amount of from about 0.001% to about 5% by weight per volume of the formulation.

49. The formulation of claim 48, wherein said amount of EDTA or a pharmaceutically acceptable salt thereof is about 0.02% to about 0.2% by weight per volume of the formulation.

50. The formulation of claim 48, wherein said amount of ethylgallate, cysteine, or ascorbic acid or a pharmaceutically acceptable salt thereof is about 0.05% to about 2% by weight per volume of the formulation.

51. The formulation of claim 42, wherein said formulation contains a concentration of total impurities of less than about 3% by weight per volume of the formulation.

52. The formulation of claim 42, wherein said formulation contains a concentration of the impurity levomepromazine sulfoxide of less than about 2% by weight per volume of the formulation.

53. The formulation of claim 46, wherein said formulation contains a concentration of total impurities of less than about 3% by weight per volume of the formulation.



54. The formulation of claim 46, wherein said formulation contains a concentration of the impurity levomepromazine sulfoxide of less than about 2% by weight per volume of the formulation.
55. The formulation of claim 42, further comprising a pH buffering agent in an amount sufficient to buffer the formulation to a pH in the range of from about 3 to about 7.
56. The formulation of claim 55, wherein said pH is in the range of from about 4 to about 5.5.
57. The formulation of claim 55, wherein said pH buffering agent comprises citric acid or a pharmaceutically acceptable salt thereof.
58. The formulation of claim 42, wherein the formulation is substantially oxygen-free.
59. The formulation of claim 42, wherein said formulation is suitable for parenteral administration.
60. The formulation of claim 59, wherein said parenteral administration comprises injection.
61. The formulation of claim 59, wherein said formulation is contained in a container selected from the group consisting of a syringe, a vial and an ampoule.

62. The formulation of claim 21, wherein  
said therapeutically effective amount of levomepromazine or a  
pharmaceutically acceptable salt thereof is about 10 mg/ml to about 30 mg/ml  
of the formulation,

EDTA or a pharmaceutically acceptable salt thereof is in an amount of  
about 0.02% to about 0.2% by weight per volume of the formulation,

MTG is in an amount of about 0.05% to 2.0% by weight per volume of  
the formulation, and

ascorbic acid or a pharmaceutically acceptable salt thereof is an amount  
of about 0.05% to about 2.0% by weight per volume of the formulation.

63. A formulation comprising

levomepromazine HCl in an amount of about 2.2% by weight per volume  
of the formulation;

ascorbic acid in an amount of about 1% by weight per volume of the  
formulation;

EDTA in an amount of about 0.065% by weight per volume of the  
formulation; and

MTG in an amount of about 1% by weight per volume of the formulation.

64. A stable terminally sterilized formulation comprising a therapeutically  
effective amount of levomepromazine or a pharmaceutically acceptable salt  
thereof, wherein said formulation contains a concentration of total impurities of  
less than about 3% by weight per volume of the formulation and is terminally  
sterillized.

65. The formulation of claim 64, wherein said concentration of the impurity levomepromazine sulfoxide is less than about 2% by weight per volume of the formulation.
66. A method for stabilizing a formulation of levomepromazine, comprising:
- (a) combining a therapeutically effective amount of levomepromazine or a pharmaceutically acceptable salt thereof, and a stabilizing amount of a combination of stabilizers in a medium to form a formulation, and
  - (b) sparging said formulation with an oxygen-free inert gas,
- wherein said combination of stabilizers comprises (1) EDTA or a pharmaceutically acceptable salt thereof as a first stabilizer and (2) monothioglycerol (MTG) or glutathione as a second stabilizer.
67. The method of claim 66, further comprising subjecting said formulation to terminal sterilization.
68. The method of claim 67, wherein said terminal sterilization comprises autoclaving.
69. The method of claim 66, wherein said gas is selected from the group consisting of nitrogen, carbon dioxide, argon, helium, and combinations thereof.
70. The method of claim 66, further comprising adding to said formulation obtained from a step (a), a pH buffering agent in an amount sufficient to buffer the formulation to a pH in the range of from about 3 to about 7.

71. The method of claim 70, wherein said pH is in the range of from about 4 to about 5.5.

72. The method of claim 70, said pH buffering agent comprises citric acid or a pharmaceutically acceptable salt thereof.

73. The method of claim 66, wherein said medium is selected from the group consisting of purified water, glucose, sterile isotonic saline, physiologically compatible organic solvents and a mixture thereof.

74. A method for stabilizing a formulation of levomepromazine, comprising:  
combining a therapeutically effective amount of levomepromazine or a pharmaceutically acceptable salt thereof, and a stabilizing amount of a combination of stabilizers in a medium suitable for parenteral administration to form a formulation,

wherein said combination of stabilizers comprises (1) EDTA or a pharmaceutically acceptable salt thereof as a first stabilizer, (2) monothioglycerol (MTG) or glutathione as a second stabilizer, and (3) ascorbic acid or a pharmaceutically acceptable salt thereof as a third stabilizer.

75. The method of claim 74, further comprising subjecting said formulation to sparging with an oxygen-free inert gas.

76. The method of claim 74 or 75, further comprising subjecting said formulation to terminal sterilization.

77. The method of claim 76, wherein said terminal sterilization comprises autoclaving.
78. The method of claim 75, wherein said gas is selected from the group consisting of nitrogen, carbon dioxide, argon, helium, and combinations thereof.
79. The method of claim 74, further comprising adding to said formulation a pH buffering agent in an amount sufficient to buffer the formulation to a pH in the range of from about 3 to about 7.
80. The method of claim 79, wherein said pH is in the range of from about 4 to about 5.5.
81. The method of claim 79, wherein said pH buffering agent comprises citric acid or a pharmaceutically acceptable salt thereof.
82. The method of claim 74, wherein said medium is selected from the group consisting of purified water, glucose, sterile isotonic saline, physiologically compatible organic solvents and a mixture thereof.
83. A method for stabilizing a formulation of levomepromazine, comprising:  
(a) combining a therapeutically effective amount of levomepromazine or a pharmaceutically acceptable salt thereof and a stabilizing amount of a combination of stabilizers in a medium suitable for parenteral administration to form a formulation, and

(b) subjecting said formulation to sparging with an oxygen-free inert gas, wherein said combination of stabilizers comprises (1) EDTA or a pharmaceutically acceptable salt thereof as a first stabilizer, (2) ethylgallate or cysteine as a second stabilizer, and (3) ascorbic acid or a pharmaceutically acceptable salt thereof as a third stabilizer.

84. The method of claim 83, further comprising subjecting said formulation to terminal sterilization.

85. The method of claim 84, wherein said terminal sterilization comprises autoclaving.

86. The method of claim 83, wherein said gas is selected from the group consisting of nitrogen, carbon dioxide, argon, helium, and combinations thereof.

87. The method of claim 83, further comprising adding to said formulation, a pH buffering agent in an amount sufficient to buffer the formulation to a pH in the range of from about 3 to about 7.

88. The method of claim 87, wherein said pH is in the range of from about 4 to about 5.5.

89. The method of claim 87, said pH buffering agent comprises citric acid or a pharmaceutically acceptable salt thereof.

90. The method of claim 83, wherein said medium is selected from the group consisting of purified water, glucose, sterile isotonic saline, physiologically compatible organic solvents and a mixture thereof.

91. A method for treating a disorder in a patient in need thereof, comprising administering to said patient an effective amount of the formulation of claim 1, wherein said disorder is selected from the group consisting of psychosis, agitation, pain, migraine headache, nausea, vomiting, itching, hypertension, benign prostatic hypertrophy, excess gastrointestinal (GI) secretions, and sleeplessness.

92. A method for treating a disorder in a patient in need thereof, comprising administering to said patient an effective amount of the formulation of claim 21, wherein said disorder is selected from the group consisting of psychosis, agitation, pain, migraine headache, nausea, vomiting, itching, hypertension, benign prostatic hypertrophy, excess gastrointestinal (GI) secretions, and sleeplessness.

93. A method for treating a disorder in a patient in need thereof, comprising administering to said patient an effective amount of the formulation of claim 42, wherein said disorder is selected from the group consisting of psychosis, agitation, pain, migraine headache, nausea, vomiting, itching, hypertension, benign prostatic hypertrophy, excess gastrointestinal (GI) secretions, or sleeplessness.